PATENT IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-006)

In the Application of:)
Fisher et al.)) Craminan F O'Horo
Serial No.: 09/882,735) Examiner: E O'Hara)
Filing Date: June 15, 2001) Group Art Unit: 1646
For: Truncated Soluble Tumor Necrosis Factor Type-I and Type-II Receptors))
CI CONTRACTOR)

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Date: May 5, 2003

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the references cited below are enclosed. These references are also listed on the enclosed PTO Form 1449.

In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief be in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned representative by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

Respectfully submitted.

McDomell Boehnen Hulbert & Berghoff

UDonald L. Zuhn

Reg. No. 48,710

Sheet 1 of 14

FORM PTO-1449	U.S. Department of Commerce	Atty. Docket No.	Serial No.
(Rev. 2-32)	Patent and Trademark Office	02-006	09/882.735
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		
	(OSC SCYCIAL SHEETS II HESSISSALY)	Applicant:	
		Fisher et al.	
		Filing Date:	Group:
		June 15, 2001	1646

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1	4,179,337	12/18/79	Davis, et al.			
	2	4,289,690	09/15/81	Pestka, et al.	_		
	3	4,522,750	6/11/85	Ades, et al.			
	4	4,560,649	12/24/85	Saxena, et al.			
	5	4,578,335	03/25/86	Urdal, et al.			
	6	4,609,546	09/02/86	Hiratani			
	7	4,670,417	06/02/87	lwasaki, et al.			
	8	4,670,563	06/02/87	Jansen, et al.			
	9	4,675,285	06/23/87	Clark, et al.			
	10	4,677,027	06/30/87	Porath, et al.			
	11	4,696,980	09/29/87	Porath			
	12	4,760,067	07/26/88	Firestone			
	13	4,766,106	08/23/88	Katre, et al.			
	14	4,789,658	12/06/88	Yoshimoto, et al.			
	15	4,791,192	12/13/88	Nakagawa, et al.			
	16	4.847,325	07/11/89	Shadle, et al.			
	17	4,902,502	02/20/90	Nitecki, et al.			
	18	4.904.584	02/27/90	Shaw			
	19	4.917.888	04/17/90	Katre, et al.			

<u></u>	 				
	20	4.931.544	06 05 90	Katre. et al.	
	21	4,935,233	06 19 90	Bell, et al.	
	22	4,959,314	09 25 90	Mark, et al.	
	23	4,966,888	10 30 90	Saxena, et al.	
	24	5,075,222	12 24 91	Hannum, et al.	
	25	5,089,261	02/18/92	Nitecki, et al.	
	26	5,093,475	03, 03 92	Carroll, et al.	
	27	5,116,964	05/26/92	Capon, et al.	
	28	5,122,614	06/16/92	Zalipsky	
	29	5,136,021	08/04/92	Dembinski, et al.	
	30	5,153,265	10/06/92	Shadle, et al.	
	31	5,162,430	11/10/92	Rhee, et al.	
	32	5,166,322	11/24/92	Shaw, et al.	
	33	5,171,264	12/15/92	Merrill	
	34	5,211,945	05/18/93	Wallach, et al.	
	35	5,214,131	05/25/93	Sano, et al.	
	36	5,252,714	10/12/93	Harris, et al.	
	37	5,344,915	09/06/94	LeMaire, et al.	
	38	5,359,032	10/25/94	Dayer, et al.	
	39	5,359,037	10/25/94	Wallach, et al.	
	40	5,382,657	01/17/95	Karasiewicz, et al.	
	41	5,395,760	03/07/95	Smith, et al.	
	42	5,446,090	08/26/95	Harris	
	43	5,453,490	09/26/95	Hageman, et al.	
	44	5,478,925	12/26/95	Wallach, et al.	
	45	5,512,544	04/30/96	Wallach, et al.	
	46	5,569,779	10/29/96	Sabahi, et al.	
	47	5,605,690	02/25/97	Jacobs, et al.	
	48	5,610,279	03/11/97	Brockhaus, et al.	
	49	5,633,145	05/27/97	Feldmann, et al.	
	50	5,681.566	10/28/97	Stevenson (English equiv. Of WO 90/04413)	
	51	5.695,953	12/09/97	Wallach, et al.	

52	5.712,155	01, 27, 98	Smith, et al.	
53	5.739,208	01, 14, 98	Harris	
54	5,747.639	05, 05, 98	Seely	
55	5.808.029	09 15/98	Brockhaus, et al.	
56	5.811,261	09/22/98	Wallach, et al.	
57	5.843.791	12/01/98	Hauptmann, et al.	
58	5,863,786	01/26/99	Feldmann, et al.	
59	5.958.409	09/28/99	Turk, et al.	

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Trans	slation
	Document Number	Date				Yes	No
60	CA 2,003,743	05/23/90	Canada				
61	DE 39 10 323 A1	10/19/89	Germany (see GB 2218101 A for English)				
62	EP 0 040 506 B1	11/25/81	Europe				
63	EP 0 092 918 A2	11/02/83	Europe				
64	EP 0 094 844 A2	11/23/83	Europe				
65	EP 0 154 316 A2	09/11/85	Europe				
66	EP 0 154 316 B1	09/13/89	Europe				
67	EP 0 169 112 B1	01/22/86	Europe (see U.S. 4,670,563 for English)				
68	EP 0 225 579 A3	06/16/87	Europe				
69	EP 0 247 860 A2	12/02/87	Europe				
70	EP 0 259 863 A2	03/16/88	Europe				
71	EP 0 308 378 A2	03/22/89	Europe			į	
72	EP 0 334 165 A2	09/27/89	Europe				
73_	EP 0 343 684 B1	11/29/89	Europe				
74	EP 0 372 752 A2	06/13/90	Europe				
75	EP 0 386 289 A1	09/12/90	Europe				
76	EP 0 393 438 A2	10/24/90	Europe (English Abstract attached)				

77	TD 0 205 952 A1	11 07 00	Lurana		
77	EP 0 395 853 A1	11,07,90	Europe		
78	EP 0 398 327 A1	11 22 90	Europe		
79	EP 0 412 486 A1	02/13/91	Europe		
80	EP 0 417 563 A2	03 20 91	Europe (see U.S. 5.610.279 for English)		
81	EP 0 418 014 A1	03/20/91	Europe		
82	EP 0 422 339 A1	04/17/91	Europe		
83	EP 0 433 900 A1	06/26/91	Europe		
84	EP 0 512 528 A2	11/11/92	Europe		
85	EP 0 526 905 A2	02/10/93	Europe		
86	EP 0 622 394 A1	11/02/94	Europe		
87	GB 2 218 101 A	11/08/89	Great Britian		
88	GB 2 246 569 A	02/05/92	Great Britian		
89	IL 90339	05/18/89	Israel		
90	JP 02040399 A	02/09/90	Japan (Abstract attached)		
91	JP 62-185029 A	08/13/97	Japan (Abstract attached)		
92	WO 87/00056 A1	01/15/87	PCT		
93	WO 88/00837 A2	02/11/88	PCT	 	
94	WO 89/05145 A1	06/15/89	PCT		
95	WO 89/06546 A1	07/27/89	PCT		
96	WO 89/09220 A1	10/05/89	PCT		
97	WO 90/04413 A1	05/03/90	PCT (see U.S. 5,681,566 for English)		
98	WO 90/04650 A1	05/03/90	PCT		
99	WO 90/05755 A1	05/31/90	PCT		
100	WO 90/12874 A2	11/01/90	PCT		
101	WO 90/13575 A1	11/15/90	PCT (see U.S. 5,344,915 for English)		
102	WO 91/03553 A1	03/21/91	PCT		
103	WO 91/05047 A1	04/18/91	PCT		
104	WO 91/07190 A1	05/30/91	PCT		
105	WO 91/16437 A1	10, 31, 91	PCT		

106	WO 92/01002 A1	01, 23, 92	PCT (abstract attached)	
107	WO 92, 01472 A1	02, 06, 92	PCT	
108	WO 92 01474 A1	02, 06, 92	PCT	
109	WO 92 04384 A1	03 19 92	PCT	
110	WO 92,07076 A1	04/30/92	PCT	
111	WO 92 13095 A1	08 ′06 ′92	PCT	
112	WO 92/15682 A1	09, 17, 92	PCT	
113	WO 92 16221 A1	10/01/92	PCT	
114	WO 92/16555 A1	10 01/92	PCT	
115	WO 93/01498 A1	01/21/93	PCT	
116	WO 94/01483 A1	01/20/94	PCT	
117	WO 94/06476 A1	03/31/94	PCT	
118	WO 95/06058 A1	03/02/95	PCT	
119	WO 95/13312 A1	05/18/95	PCT	
120	WO 95/34326 A1	12/21/95	PCT	
121	WO 96/19459 A1	06/27/96	PCT	
122	WO 97/32607 A2	09/12/97	PCT	

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

123	Abuchowski, et al., "Effect of Covalent Attachment of Polyethylene Glycol on Immunogenicity and Circulating Life of Bovine Liver Catalase," <i>Journal of Biological Chemistry</i> , 252 (11): 3582-3586 (1977).
124	Aggarwal, et al., "Characterization of Receptors for Human Tumour Necrosis Fator and Their Regulation by γ-Interferon", Nature, 318: 665-667 (1985).
125	Akerblom, et al., "Preparation and Characterization of Conjugates of Monoclonal Antibodies and Staphylococcal Enterotoxin A Using a New Hydrophilic Cross-Linker," <i>Bioconjugate Chem.</i> , 4:455-466 (1993).
126	Anderson, et al., "Quantitative Filter Hybridisation," Nucleic Acid Hybridization: A Practical Approach, Hawes, et al. (ed)., pp. 73-111 (1985).
127	Ashkenazi, et al., "Protection Against Endotoxic Shock by a Tumor Necrosis Factor Receptor Immunoadhesin," <i>PNAS</i> 88: 10535-10539 (1991).
128	Baglioni, et al., "Binding of Human Tumor Necrosis Factor to High Affinity Receptors on HeLa and Lymphoblastoid Cells Sensitive to Growth Inhibition," <i>Journal of Biological Chemistry</i> , 260 (25): 13395-13397 (1985).
129	Baker, et al., "Inhibition of EAE by TNF-Receptor Fusion Proteins," <i>J. Neuroimmunology</i> , 54 (1-2): 151 Abstract P16.01 (1992).
130	Bakouche, et al., "Plasma Membrane-Associate Tumor Necrosis Factor, A Non-Integral Membrane Protein

		Possibly Bound to Its Own Receptor". J. Immunol. 140: 1142-1147 (1988).
	131	Banner, et al., "Crystal Structure of the Soluble Human 55 KD TNF Receptor-Human TNFB Complex: Implications for TNF Receptor Activation", <i>Cell.</i> , 73: 431-445 (1993).
	132	Beutler, et al., "Passive Immunization against Cachectin/Tumor Necrosis Factor Protects Mice from Lethal Effect of Endotoxin", Science, 229:869-871 (1985).
	133	Beutler and Cerami, "The Biology of Cachectin/TNF-A Primary Mediator of the Host Response", Ann. Rev. Immunol., 7:625-655 (1989).
	134	Bevilacqua, et al., "Recombinant tumor necrosis factor induces procoagulant activity in cultured human vascular endothelium: Characterization and comparison with the actions of interleukin 1," <i>Proc. Natl. Acad. Sci. USA</i> , 83: 4533-4537 (1986).
	135	Binkert, et al., "Cloning, Sequence Analysis and Expression of a cDNA Encoding a Novel Insulin-like Growth Factor Binding Protein (IGFBP-2)," The <i>EMPO J.</i> 8 (9):2497-2502 (1989).
	136	Bourdon, et al., "Structure-function Relationships of Hirulog Peptide Interactions with Thrombin," FEBS 294:163-166 (1991).
	137	Bowie, et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," <i>Science</i> , 247: 1306-1310 (1990).
	138	Brakebusch, et al., "Diverse Functions of the Tumor Necrosis Factor Receptors: Structure-Activity Considerations," <i>Tumor Necrosis Factor: Molecular and Cellular Biology and Clinical Relevance</i> , pp. 40-51 (1993).
	139	Brennan, et al., "Inhibitory Effect of the TNF α Antibodies on Synovial Cell Interleukin-1 Production in Rheumatoid Arthritis," Lancet, vol. 2 (8657), pp. 224-247 (1989).
	140	Brockhaus, et al., "Identification of Two Types of Tumor Necrosis Factor Receptors on Human Cell Lines by Monoclonal Antibodies," <i>Proc. Natl. Acad. Sci. USA</i> , 87:3127-3131 (1990).
	141	Butler, et al., "TNF Receptor Fusion Proteins are Effective Inhibitors of TNF-Mediated Cytotoxicity on Human KYM-1D4 Rhabdomyosarcoma Cells," <i>Cytokine</i> , 6 (6): 616-623 (1994).
	142	Byrn, et al., "Biological Properties of a CD4 Immunoadhesin," Nature (London) 344:667-670 (1990).
į	143	Capaldi, et al., "Changes in Order of Migration of Polypeptides in Complex III and Cytochrome & Oxidase under Different Conditions of SDS Polyacrylamide Gel Electrophoresis," <i>Biochem. & Biophys. Res Comm.</i> 74 (2):425-433 (1977).
	144	Carlino, et al., "Use of a Sensitive Receptor Binding Assay to Discriminate Between Full-Length and Truncated Human Recombinant TNF Proteins," <i>J. Biol. Chem.</i> 262 (3):958-961 (1987).
	145	Carrieri, et al., "Cytokines in the Pathogenesis of Multiple Sclerosis," <i>Acta Neurologica</i> , 14 (4-6): pp. 333-341 (1992).
	146	Chaudhary, et al., "A Recombinant Immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin," <i>Nature</i> , 339:394-397 (1989).
	147	Chen, et al., "Production of Multimeric Forms of CD4 Through a Sugar-based Cross linking Strategy," J. Biol. Chem., 266 (27): 18237-18243 (1991).
	148	Chih-Hsueh Chen P., et al., "Mapping the Domain(s) Critical for the Binding of Human Tumor Necrosis Factor-Alpha to its Two Receptors," <i>The Journal of Biological Chemistry</i> , 240 (6): 2874-2878 (Feb. 10, 1995).
	149	Colletti, et al., "The Production of Tumor Necrosis Factor Alpha and the Development of a Pulmonary Capillary Injury Following Hepatic Ischemia/Reperfusion." <i>Transplantation</i> 49 (2): 268-272 (1990).

150	Conforti, et al., "PEG Superoxide Dismutase Derivatives: Anti-inflammatory Activity in Carrageenan Pelurisy in Rats," <i>Pharmacological Research Communications</i> , 19 (4): 287-294 (1987).
151	Corcoran, et al., "Characterization of Ligand Binding by the Human p55 Tumor-Necrosis-Factor Receptor Involvement of Individual Cysteine-Rich Repeats," <i>Eur. J. Biochem.</i> , 223:831-840 (1994).
152	Creasey, et al., "A High Molecular Weight Component of the Human Tumor Necrosis Factor Receptor is Associated with Cytotoxicity," <i>Proc. Natl. Acad. Sci. USA</i> , 84: 3293-3297 (1987).
153	Davis, et al., "Soluble, nonantigenic Polyethylene Glycol-Bound Enzymes," <i>Biomedical Polymers: Polymeric Materials and Pharmaceuticals for Biomedical Use</i> , Goldberg, et al. (Ed.), published by Academic Press (NY), pp. 441-452 (1980).
154	Dayer, et al., "Purification and Characterization of Human Tumor Necrosis Factor α Inhibitor," Chemical Abstracts, 113 (38760n): 454 (1990).
155	Dayer, et al., "Interleukin-1, Tumor Necrosis Factor and Their Specific Inhibitors," European Cytokine Network, 5 (6): 563-571.
156	Delgado, et al., "The Uses and Properties of PEG-Linked Proteins." Critical Reviews in Therapeutic Drug Carrier Systems, 9 (3,4): 249-304 (1992).
157	Dembic, et al., "Two Human TNF Receptors Have Similar Extracellular, But Distinct Intracellular, Domain Sequences," <i>Cytokine</i> , 2 (4): 231-237 (1990).
158	Dohlsten, et al., "Monoclonal Antibody-targeted Superantigens: A Different Class of Anti-tumor Agents," <i>Proc. Natl. Acad. Sci. USA</i> , 88: 9287-9291 (1991).
159	Eisenberg, et al., "Primary Structure and Functional Expression from complementary DNA of a Human Interleukin-1 Receptor Antagonist," <i>Nature</i> , 343: 341-346 (1990).
160	Elliott, et al., "Randomised Double-blind Comparison of Chimeric Monoclonal Antibody to Tumour Necrosis Factor α (cA2) versus Placebo in Rheumatoid Arthritis," <i>Lancet</i> , 344: 1105-1110 (1994).
161	Englemann, et al., "A Tumor Necrosis Factor-Binding Protein Purified to Homogeneity from Human Urine Protects Cells from Tumor Necrosis Factor Toxicity," <i>J. Biol. Chem.</i> , 264 (20): 11974-11980 (1989).
162	Englemann, et al., "Antibodies to a Soluble Form of a Tumor Necrosis Factor (TNF) Receptor have TNF Like Activity," Journal of Biological Chemistry, 265 (24): 14497-14504 (1990).
163	Englemann, et al., "Two Tumor Necrosis Factor-Binding Proteins Purified From Human Urine," <i>J. Biol. Chem.</i> , 265 (3): 1531-1536 (1990).
164	Erez, et al., "Narcotic Antagonistic Potency of Bivalent Ligands Which Contain β-Naltrexamine Evidence for Bridging Between Proximal Recognition Sites," <i>J. Med. Chem.</i> , 25: 847-849 (1982).
165	Espevik, et al., "Characterization of Binding and Biological Effects of Monoclonal Antibodies Against a Human Tumor Necrosis Factor Receptor," <i>Journal Exp. Med.</i> , 171: 415-426 (1990).
166	Evans, Ronald M., "The Steroid and Thyroid Hormone Receptor Superfamily," Science 240: 889-895 (1998).
167	Feldman, et al., "Receptor Activation by Antigens, Cytokines, Hormones, and Growth Factors," Annals of The New York Academy of Sciences, 766: 272-278 (1995).
168	Fisher, et al., "Treatment of Septic Shock with the Tumor Necrosis Factor Recptor: Fc Fusion Protein," The New England Journal of Medicine, 334 (26): 1697-1702 (1996).
169	Frohman, et al., "Rapid production of full-length cDNAs from rare transcripts: Amplification using a single gene-specific oligonucleoide primer." <i>Proc. Natl. Acad. Sci.</i> USA 85: 8998-9002 (1988).
170	Fu ZQ.: "Model Complexes of Tumor Necrosis Factor-Alpha with Receptors R1 and R2," Protein

,	Τ	5
	ļ	Engineering, 8 (12): 1233-1241 (1995).
	171	Gatanaga, et al., "Purification and Characterization of an Inhibitor (Soluable Tumor Necrosis Factor Receptor) for Tumor Necrosis Factor and Lymphotoxin Obtained from the Serum Ultrafiltrates of Human Cancer Patients," <i>Proc National Academy of Science</i> USA 87: 8781-8784.
	172	Glass, et al., "4-Phenoxy-3, 5-Dinitrobenzoylpolyethyleneglycol: Reversible Attachment of Cysteine-Containing Polypeptides to Polymers in Aqueous Solutions," <i>Biopolymers</i> , 18: 383-392 (1979).
	173	Goodson, et al., "Site-Directed Pegylation of Recombinant Interleukin-2 At Its Glycosylation Site," BioTechnology, 8: 343-346 (1990).
	174	Goodwin, et al., "Molecular Cloning and Expression of the Type 1 and Type 2 Murine Receptors for Tumor Necrosis Factor," <i>Molecular and Cell Biology</i> 11 (6): 3020-3026 (1991).
	175	Gray, et al., "Cloning of Human Tumor Necrosis Factor (TNF) Receptor cDNA and Expression of Recombiant soluble TNF-Binding Protein," <i>Proc. Natl. Acad. Sci. USA</i> , 87 (19): 7380-7384 (1990).
	176	Grizzard, et al., "Affinity-Labeled Somatomedin-C Receptors and Binding Proteins From the Human Fetus." Journal of Clinical Endocrinology and Metabolism, 58 (3): 535-543 (1984).
	177	Hale, et al., Cytokines and Their Receptors: From Clonal to Clinical Investigation-"Demonstration of in Vitro and in Vivo Efficacy of Two Biologically Active Human Soluble TNF Receptors Expressed in E. Coli," J. Cell. Biochem., Suppl. 15F: 113 (1991).
	178	Hannum, et al., "Interleukin-1 Receptor Antagonist Activity of a Human Interleukin-1 Inhibitor," <i>Nature</i> , 343 (6256): 336-340 (1990).
	179	Harris Milton, "Laboratory Synthesis of Polyethylene Glycol Derivatives," Rev. Macromol. Chem. Phys., 25 (3): 325-373 (1985).
	180	Harris, et al., "Synthesis and Characterization of Poly (ethylene Glycol) Derivatives," Journal of Polymer Science: Polymer Chemistry Edition. 22: 341-352 (1984).
	181	Hass, et al., "Characterization of Specific High Affinity Receptors for Human Tumor Necrosis Factor on Mouse Fibroblasts," <i>J. Biol. Chem.</i> 260(22): 12214-12218 (1985).
	182	Hatakeyama, et al., "Interleukin-2 Receptor β Chain Gene: Generation of Three Receptor Forms by Cloned Human α and β Chain cDNA's," <i>Science</i> 244: 551-556 (1989).
	183	Hauser, et al., "Cytokine Accumulations in CSF of Multiple Sclerosis Patients: Frequent Detection of Interleukin-1 and Tumor Necrosis Factor but not Interleukin-6," <i>Neurology</i> 40: 1735-1739 (1990).
	184	Heller, et al., "Amplified Expression of Tumor Necrosis Factor Receptor in Cells Transfected with Espstein-Barr Virus Shuttle Vector cDNA Libraries," <i>J. Biol. Chem.</i> , 265 (10): 5708-5717 (1990).
	185	Heller, et al., "Complementary DNA Cloning of a Receptor for Tumor Necrosis Factor and Demonstration of a Shed Form of the Receptor," <i>Proc. Natl. Acad. Sci. USA</i> , 87: 6151-6155 (1990).
	186	Himmler, et al., "Molecular Cloning & Expression of Human & Rat Tumor Necrosis Factor Receptor Chain (p 60) and its Soluable Derivative, Tumor Necrosis Factor-Binding Protein." DNA and Cell Biology, 9 (10): 705-715 (1990).
	187	Hoes, et al., "Optimization of Macromolecular Prodrugs of the Antitumor Antibiotic Adriamycin," <i>Journal of Controlled Release</i> . 2: 205-213 (1985).
	188	Hofman, et al., "Tumor Necrosis Factor Identified in Multiple Sclerosis Brain." J. Exp. Med. 170: 607-612 (1989).
	189	Hohmann, et al., "Two Different Cell Types Have Different Major Receptors for Human Necrosis Factor (TNF α)," Journal of Biol. Chem. 264: 14927-14934 (1989).

190	Horner, et al., "Aryl-vinlysulfone-reagentien Zum Shutz Und Nacheweis Von Thiofunkitonen," <i>Phosphorus and Sulfur</i> 15: 1-8 (1983).
191	Israel, et al., "Binding of Human TNF- α to High-Affinity Cell Surface Receptors: Effect of IFN," <i>Immunol</i> , Lett. 12: 217-224 (1986).
192	Jenkins, et al., "Tumor Necrosis Factor Causes an Increase in Axonal Transport of Protein and Demyelination in the Mouse Optic Nerve," <i>Journal of Neurological Sciences</i> , 108: 99-104 (1992).
193	Jiang, et al., "Defined Chemically Cross-Linked Oligomers of Human C-Reactive Protein: Characterization and Reactivity with the Complement System," <i>Immunology</i> , 74: 725-731 (1991).
194	Johansson, Gote, "Studies on Aqueous Dextran-Poly (Ethylene Glycol) Two-Phase Systems Containing Charged Poly (Ethylene Glycol)," <i>Giochimica Et Biophysica Acta</i> , 222: 381-389 (1970).
195	Kalli, et al., "Mapping of the C3b-binding Site of CR 1 and Construction of a (CR 1) ₂ -F(ab ¹) ₂ Chimeric Complement Inhibitor," <i>J. Exp. Med.</i> 174: 1451-1460 (1991).
196	Kasukabe, et al., "Purification of a Novel Growth Inhibitory Factor for Partially Differentiated Myeloid Leukemic Cells," <i>Journal of Biol. Chem.</i> 263 (11): 5431-5435 (1988).
197	Katre, et al., "Chemical Modification of Recombinant Interleukin 2 by polyethylene glycol increases its potency in the murine Meth A Sarcome model," <i>Proc. Natl. Acad. Sci. USA</i> , 84:1487-1491 (1987).
198	Knauf, et al., "Relationship of Effective Molecular Size to Systematic Clearance in Rats of Recombinant Interleukin-2 Chemically Modified with Water-soluble Polymers," <i>The Journal of Biological Chemistry</i> , 263 (29): 15064-15070 (1988).
199	Kogan, Timothy, "The Synthesis of Substituted Methoxy-Poly (EthyleneGlycol) Derivatives Suitable for Selective Protein Modification," Synthetic Communications, 22 (16): 2417-2424 (1992).
200	Kohgo, et al., "Circulating Transferrin Receptor in Human Serum," British Journal of Haematology, 64: 277-281 (1986).
201	Kohno, et al., "A Second Tumor Necrosis Factor Receptor Gene Product Can Shed a Naturally Occurring Tumor Necrosis Factor Inhibitor," <i>Proc. Natl. Acad. Sci. USA</i> , 87: 8331-8335 (1990).
202	Kull, et al., "Cellular Receptor for ¹²⁵ l-Labeled Tumor Necrosis Factor: Specific Binding, Affinity Labeling, and Relationship to Sensitivity," <i>Proc. Natl. Acad. Sci. USA</i> , 82: 5756-5760 (1985).
203	Kuroki, et al., "Aryl Vinyl Sulfones as Thiol Protective Group," Tetrahedron Letters, 25 (2): 197-200 (1984).
204	Lantz, et al., "Characterization <i>In Vitro</i> of Human Tumor Necrosis Factor-Binding Protein," <i>J. Clin. Invest.</i> , 86: 1396-1402 (1990).
205	Le, et al., "Tumor Necrosis Factor and Interleukin 1: Cytokines with Multiple Overlapping Biological Activities," Lab Investigation 56 (3): 234-248 (1987).
206	Lee, et al., "Generation of cDNA Probes Directed by Amino Acid Sequence: Cloning of Urate Oxidase Science 239: 1288-1291 (1988).
207	Lehmann, et al., "Demonstration of Membrane Receptors for Human Natural Recombinant ¹²⁵ I-Labeled Tumor Necrosis Factor on HeLa Cell Clones and Their Role in Tumor Cell Sensitivity," <i>Eur. J. Biochem.</i> 158: 1-5 (1986).
208	Leung, et al., "Growth Hormone Receptor and Serum Binding Protein: Purification, Cloning and Expression." <i>Nature</i> 330:537-543 (1987).
209	Liao, et al., "Characterization of a Human Interleukin 1 Inhibitor," J. Immunol., 134 (6): 3882-3886 (1985).
210	Liao, et al., "Identification of a Specific Interleukin 1 Inhibitor in the Urine of Febrile Patients," J. Exp. Med.

	159: 126-136 (1984).
211	Liblau, et al., "Tumor Necrosis Factor- α and Disease Progression in Multiple Sclerosis," New Engl. J. Med. 326 (4): 272-273 (1992).
212	Lindvall, et al., "Modulation of the Constitutive Gene Expression of the 55 KD Tumor Necrosis Factor Receptor in Hematopoietic Cells," <i>Biochem. & Biophys. Res. Comm.</i> 172 (2) 557-563 (1990).
213	Loetscher, et al., "Molecular Cloning Expression of the Human 55kd TNF Necrosis Factor Receptor," <i>Cell</i> , 61: 351-359 (1990).
214	Loetscher, et al., "Recombinant 55-kDa Tumor Necrosis Factor (TNF) Receptor," <i>J. Biol. Chem.</i> 266(27): 18324-18329 (1991).
215	Marangonore, et al., "Design and Characterization of Hirulogs: A Novel Class of Bivalent Peptide Inhibitors of Thrombin," <i>Biochemistry</i> , 29: 7095-7101 (1990).
216	March, et al., "Cloning, Sequence and Expression of Two Distinct Human Interleukin-1 Complementary DNAs," Nature 315: 641-647 (1985).
217	Marsters S.A., et al., "Identification of Cystein-Rich Domains of the Type 1 Tumor Necrosis Factor Receptor Involved in Ligand Binding," The Journal of Biological Chemistry, 267 (9): 5747-5750 (March 25, 1992).
218	Martin, et al., "Inhibition of Tumor Necrosis Factor is Protective Against Neurologic Dysfunction After Active Immunization of Lewis Rats with Myelin Basic Protein," Exp. Neurol, 131: 221-228 (1995).
219	McFarland, Henry, "Therapeutic Approaches to Multiple Sclerosis," <i>J. Neurochem.</i> , 64 (Suppl.): S73 (Abstract C) (1995).
220	Monastra, et al., "Phosphatidylserine, a Putative Inhibitor of Tumor Necrosis Factor, Prevents Autoimmune Demyelination," <i>Neurology</i> , 43: 153-163 (1993).
221	Murata, et al., "Ingibitory Effect of a Synthetic Polypeptide, poly(Tyr-Ile-Gly-Ser-Arg), On the Metastatic Formation of Malignant Tumour Cells," Int. J. Biol. Macromol., 11:97-99 (1989).
222	Neda, Hiroshi, "Analysis of the Tumor Necrosis Factor (TNF) Receptor of Various Tumor Cells," Sapporo Medical Journal, 56 (2): 305-317 (1987).
223	Nexo, et al., "Lectin-Agarose Immobilization, a New Method for Detecting Soluble Membrane Receptors," J. Biol. Chem. 254 (18): 8740-8743 (1979).
224	Nophar, et al., "Soluble forms of tumor necrosis factor receptors (TNF-Rs). The cDNA for the type I TNF-R, cloned using amino acid sequence data of its soluble form, encodes both the cell surface and a soluble form of the receptor," <i>The EMBO J.</i> , 9 (10): 3269-3278 (1990).
225	Novick, et al., "Soluble Cytokine Receptors are Present in Normal Human Urine." J. Exp. Med. 170: 1409-1414 (1989).
226	Novick, et al., "Soluble Cytokine Receptors are Present in Normal Human Urine," The Physiological and Pathological Effects of Cytokines, pp. 413-421 (1990).
227	Novick, et al., "Purification of Soluble Cytokine Receptros from Normal Human Urine by Ligand-Affinity and Immunoaffinity Chromatography," <i>J. Chromatog.</i> 510: 331-337 (1990).
228	Oliff, et al., "Tumors Secreting Human TNF/Cachectin Induce Cachexia In Mice." Cell. 50: 555-563 (1987).
229	Olsson, et al., "Isolation and Characterization of a Tumor Necrosis Factor Binding Protein from Urine," Eur. J. Haematology, 42 (3): 270-275 (1989).
230	Paleolog, et al., "Deactivation of Vascular Endothelium By Monoclonal Anti-Tumor Necrosis Factor α Antibody in Rheumatoid Arthritis." Arthritis and Rheumatism. 39:1082-1091 (1996).

	231	Peetre, et al., "A Tumor Necrosis Factor Binding Protein is Present in Human Biological Fluids," Eur. J. Haematology, 41: 414-419 (1988).
	232	Pennica, et al., "Biochemical Properties of the 75-kDa Tumor Necrosis Factor Receptor," Journal of Biological Chemistry, 267 (29): 21172-21178 (1992).
	233	Peppel, et al., "A Tumor Necrosis Factor (TNF) Receptor-IgG Heavy Chain Chimeric Protein as a Bivalent Antagonist of TNF Activity," <i>J. Exp. Med.</i> , 174: 1483-1489 (1991).
234		Piguet, et al., "Tumor Necrosis Factor/Cachectin Plays a Key Role in Bleomycin-Induced Pneumophathy and Fibrosis," J. Exp. Med., 170: 655-663 (1989).
	235	Portoghese, et al., "Opioid Agonist and Antagonist bivalent Ligands. The Relationship Between Spacer Length and Selectivity at Multiple Opioid Receptors," <i>J. Med. Chem.</i> , 29: 1855-1861 (1986).
	236	Powell, et al., "The Role of Lymphotoxin and TNF in Demyelinating Diseases of the CNS," <i>Tumor Necrosis Factors: The Molecules and Their Emerging Role in Medicine</i> , ed. By B. Beutler, Raven Press, New York, pp. 355-369 (1992).
	237	Powell, et al., "Lymphotoxin and Tumor Necrosis Factor-Alpha Production by Myelin Basic Protein-Specific T Cell Clones Correlates with Encephalitogenicity," <i>International Immunology</i> , 2 (6): 539-544 (1990).
	238	Rankin, et al., "The Therapeutic Effects of an Engineered Human Anti-Tumour Necrosis Factor Alpha Antibody (CDP571) in Rheumatoid Arthritis," <i>British Journal of Rheumatology</i> , 34: 334-342 (1995).
	239	Rhein, Reginald., "Another Sepsis Drug Down-Immunex' TNF Receptor," Biotechnology <i>Newswatch</i> , pp. 1-3 (Monday, October 4, 1993).
	240	Romani, et al., "Synthesis of unsymmetrical Cystine Peptides: Directed Disulfide Pairing with the Sulfenohydrazide Method," <i>Chemistry of Peptides and Proteins</i> , 2: 29-34 (1984).
	241	Rosenstreich, et al., "A Human Urine-Derived Interleukin 1 Inhibitor," J. Exp. Med., 168: 1767-1779 (1988).
	242	Ruddle, et al., "An Antibody to Lympotoxin and Tumor Necrosis Factor Prevents Transfer of Experimental Allergic Encephalomyelitis," <i>J. Exp. Med.</i> 172: 1193-1200 (1990).
	243	Scallon, et al., "Functional Comparisons of Different Tumor Necrosis Factor Receptor/lgG Fusion Proteins," <i>Cytokine</i> , 7(8): 759-770 (1995).
	244	Schall, et al., "Molecular Cloning and Expression of a Receptor for Human Tumor Necrosis Factor," <i>Cell</i> , 61: 361-370 (1990).
	245	Scheurich, et al., "Quantification and Characterization of High-Affinity Membrane Receptors for Tumor Necrosis Factor on Human Leukemic Cell Lines," <i>Int. J. Cancer</i> 38 (1): 127-133 (1986).
	246	Seckinger, et al., "A Human Inhibitor of Tumor Necrosis Factor Alpha," <i>J. Exp. Med.</i> , 167: 1511-1516 (1988).
	247	Seckinger, et al., "A Urine Inhibitor of Interleukin 1 Activity Affects Both Interleukin 1 α and 1 β But Not Tumor Necrosis Factor α ," J. Immunol. 139 (5): 1541-1545 (1987).
	248	Seckinger, et al., "Characterization of a Tumor Necrosis Factor α (TNF- α) Inhibitor: Evidence of Immunological Cross-Reactivity with the TNF Receptor," <i>Proc. Natl. Acad. Sci. USA</i> , 87: 5188-5192 (1990).
	249	Seckinger, et al., "Purification and Biologic Characterization of a Specific Tumor Necrosis Factor α Inhibitor," J. Biol. Chem., 264 (20): 11966-11973 (1989).
	250	Seckinger, et al., "A Urine Inhibitor of Interleukin 1 Activity That Blocks Ligand Binding," <i>J. Immunol.</i> , 139 (5): 1546-1549 (1987).
	251	Seely, et al., "Manufacturing of Recombinant Tumor Necrosis Factor Binding Protein 'Dumbell' Using a 20K

	PEG BIS Vinylsulfone Linker," 209 Am. Chem. Soc. National Meeting, Anaheim, Cal., April 2-6 1995, BIOT 68.
252	Selby, et al., "Endogeneous Tumor Necrosis Factor in Cancer Patients," Lancet, 1 (8583): 483 (1988).
253	Selmaj, et al., "Anti-Tumor Necrosis Factor Therapy Abrogates Autoimmune Demyelination," <i>Annals of Neurology by Am. Neurol. Assoc.</i> , 30 (5): 694-700 (1991).
254	Selmaj, et al., "Prevention of CHR-EAE with Soluble TNF Receptor P55," <i>J. Neuroimmunology</i> , 54 (12): 196. Abstract W15.05 (1994).
255	Selmaj, et al., "Prevention of Chronic Relapsing Experimental Autoimmune encephalomyelitis by Soluble Tumor Necrosis Factor Receptor I," <i>J. Neuroimmunology</i> , 56: 135-141 (1995).
256	Selmaj, et al., "Proliferation of Astrocytes in Vitro in Response to Cytokines: A Primary Role for Tumor Necrosis Factor," <i>J. Immunol.</i> 144 (1): 129-135 (1990).
257	Selmaj, et al., "Tumor Necrosis Factor Mediates Myelin and Oligodendrocyte Damage in Vitro," <i>Annals of Neurology</i> 23(4): 339-346 (1998).
258	Sharief, et al., "Association Between Tumor Necrosis Factor-Alpha and Disease Progression in Patients with Multiple Sclerosis," New England J of Med. 325 (7): 467-472 (1991).
259	Shimohigashi, et al., "Dimeric Tetrapeptide Enkephalins Display Extraoridinary Selectivity for the δ Opiate Receptor," <i>Nature</i> , 297: 333-335 (1982).
260	Smith, Craig, "cDNA Expression: Cloning of the Receptor for Human Tumor Necrosis Factor," Presentation Programme, 29 th Midwinter Conference of Immunologists (January 27-30, 1990).
261	Smith, Craig, "cDNA Expression: Cloning of the Receptor for Human Tumor Necrosis Factor," Presentation at the 29 th Midwinter Conference of Immunologists (January 27-30, 1990).
262	Smith, et al., "A Receptor for Tumor Necrosis Factor Defines as unusual Family of Cellular and Viral Proteins," <i>Science</i> , 248: 1019-1023 (1990).
263	Smith, et al., "A Receptor for Tumor Necrosis Factor Defines an Unusual Family of Cellular and Viral Proteins," Genbank database excerpt released after publication (May 1990).
264	Smith, et al., "Species Specificity of Human and Murine Tumor Necrosis Factor," J. Biol. Chem., 261 (32): 14871-14874 (1986).
265	Socher, et al., "Antibodies Against Amino Acids 1-15 of Tumor Necrosis Factor Block Its Binding Cell-Surface Receptor," <i>Proc. Natl. Acad. Sci.</i> USA 84: 8829-8833 (1987).
266	Spinas, et al., "Induction of Plasma Inhibitors of Interleukin 1 and TNF-Alpha Activity by Endotoxin Administration to Normal Humans," <i>Am. J. Physiol.</i> 259: R993-R997 (1990).
267	Starnes, Jr., et al., "Tumor Necrosis Factor and the Acute Metabolic Response to Tissue Injury in Man," 82: 1321-1325 (1988).
268	Stauber, et al., "Human Tumor Necrosis Factor-a Receptor," J. Biol. Chem., 263 (35): 19098-19104 (1988).
269	Stauber, et al., "Characterization and Affinity Cross-Linking of Receptors for Human Recombinant Lymphotoxin (Tumor Necrosis Factor- β) on a Human Histiocytic Lymphoma Cell Line U-937," J. Biol. Chem. 264 (6): 3573-3576 (1989).
270	Suffys. et al., "Involvement of a Serine Protease in Tumour-Necrosis-Factor-Mediated Cytotoxicity," Eur. J. Biochem. 178: 257-265 (1988).
271	Suggs, et al., "Use of Synthetic Oligonucleotides as Hybridization Probes: Isolation of Cloned cDNA Sequences for Human β2-Microglobulin," <i>Proc. Natl. Acad. Sci.</i> U.S.A. 78(11): 6613-6617 (1981).

272	Suzuki, et al., "Physicochemical and Biological Properties of Poly (Ethylene Glycol)-Coupled Immunoglobulin G." <i>Biochimica et Biophysica Acta.</i> , 788: 248-255 (1984).
273	Tak, et al., "Decrease in Cellularity and Expression of Adhesion Molecules by Anti-tumor Necrosis Factor α Monoclonal Antibody Treatment in Patients with Rheumatoid Arthritis," <i>Arthritis and Rheumatism</i> , 39: 1077-1081 (1996).
274	The Cytokine Factsbook, Callard (ed.), Academic Press, Inc., San Diego, CA., pp. 244-246 (1994).
275	Tracey, et al., "Anti-Cachectin/TNF Monoclonal Antibodies Prevent Septic Shock During Lethal Bacteraemia," <i>Nature</i> 330: 662-664 (1987).
276	Tracey, et al., "Cachectin/Tumor Necrosis Factor Induces Cachexia, Anemia, and Inflammation," J. Exp. Med. 167: 1211-1227 (1988).
277	Tracey, et al., "Metabolic Effects of Cachectin/Tumor Necrosis Factor Are Modified by Site of Production." <i>J. Clon Invest.</i> 86: 2014-2024 (1990).
278	Tracey, et al., "Physiological Responses to Cachectin," Tumor necrosis factor and related cytotoxins. Wiley, Chichester (Ciba Foundation Symposium 131), pp. 88-108 (1987).
279	Tsujimoto, et al., "Characterization and Affinity Crosslinking of Receptors for Tumor Necrosis Factor on Human Cells," <i>Archives of Biochem. & Biophys.</i> 249 (2): 563-568 (1986).
280	Unglaub, et al., "Downregulation of Tumor Necrosis Factor (TNF) Sensitivity Via Modulation of TNF Binding Capacity by Protein Kinase C Activators," <i>J. Exp. Med.</i> 166: 1788-1797 (1987).
281	Van Zee, et al., "Tumor Necrosis Factor Soluble Receptors Circulate During Experimental and Clinical Inflammation and Can Protect Against Excessive Tumor Necrosis Factor α In Vitro and In Vivo," Proc. Natl. Acad. Sci. USA, 89: 4845-4849 (1992).
282	Vilcek, et al., "Tumor Necrosis Factor: Receptor Binding and Mitogenic Action in Fibroblasts," Journal of Cellular Physiology Supplement 5: 57-61 (1987).
283	Vitt, et al., "Biological and Structural Characterization of the Tumor Necrosis Factor Receptor on Multiple Cell Types: Relationship to Function," Fed. Proc. 78 th Annual Meeting of the American Society of Biological Chemists 46 (6): 2117 (Abstract 1118) (1987).
284	Waage, et al., "Association Between Tumour Necrosis Factor in Serum and Fatal Outcome in Patients with Meningococcal Disease," <i>Lancet</i> , 1 (8529): 355-357 (1987).
285	Wallach, et al., "Cell Surfae and Soluable TNF Receptors," Tumor Necrosis Factor: Structure-Function Relationship and Clinical Application, Osawa T, Bonavida B (eds), Karger, Basel. 47-57 (1992).
286	Wallach, et al., "Mechanisms Which Take Part in Regulation of the Response to Tumor Necrosis Factor," Lymphokine Research 8 (3): 359-363 (1989).
287	Wallach, David, "Preparations of Lymphotoxin Induce Resistance to Their Own Cytotoxic Effect," <i>J. Immunol.</i> 132 (5): 2464-2469 (1984).
288	Wallach, et al., "Regulation of the Response to Tumor Necrosis Factor," <i>Tumor Necrosis Factor/Cachectin and Related Cytokines Int. Conf.</i> , <i>Heidelberg 1987</i> , Tumor Necrosis Factor Related Cytotoxins, Bonavida, Gifford, Kirchner, Old (eds), Karger, Basel. Pp. 134-147 (1988).
289	Walsh, et al., "Isolation and Purification of ILS, an Interleukin 1 Inhibitor Produced by Human Gingival Epithelial Cells," Clin. Exp. Immunol. 68: 366-374 (1987).
290	Weber, et al., "Production of an Epidermal Growth Factor Receptor-Related Protein," <i>Science</i> 224: 294-297 (1984).
29	Weisman, et al., "Soluble Human Complement Receptor Type I: In Vivo Inhibitor of Complement Suppressing

		Post-Ischemic Myocardial Inflammation and Necrosis." Science, 249: 146-151 (1990).		
	292	Yoshie, et al., "Binding and Crosslinking of 125I-Labeled Recombianant Human Tumor Necrosis Factor to Ce Surface Receptors," J. Biochem. 100: 531-541 (1986).		
	293	Zalipsky. Samuel. "Synthesis of an End-Group Functionalized Polyethylene Glycol-Lipid Conjugate for Preparation of Polymer-Grafted Liposomes." <i>Bioconjugate Chem.</i> , 4: 296-299 (1993).		
	294	Zeigler, Elizabeth J., "Tumor Necrosis Factor in Humans," New Engl. J. Med. 318 (23): 1533-1535 (1988).		
EXAMINER			DATE CONSIDERED	

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-006)

In the	Application of:)
)
	Fisher et al.)
) Examiner: E O'Hara
Serial	No.: 09/882,735)
) Group Art Unit: 1646
Filing	Date: June 15, 2001)
)
For:	Truncated Soluble Tumor Necrosis Factor)
	Type-I and Type-II Receptors)
)

TRANSMITTAL LETTER

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

In regard to the above identified application.

- 1. We are transmitting herewith the attached:
 - a) Information Disclosure Statement:
 - b) PTO Form 1449; and cited references
 - c) Return postcard
- 2. With respect to fees:

Date: May 5, 2003

- a) No fees are required
- b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.
- 3. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage Express Mail in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231 on May 5, 2003.

Respectfully submitted.

Donald L. Zuhn

Registration No. 48/10